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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/660,118	09/10/2003	Carl W. White	2879-98	7778

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EXAMINER	
MOHAMED, ABDEL A	
ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 03/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/660,118	WHITE, CARL W.	
	Examiner	Art Unit	
	Abdel A. Mohamed	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 February 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/1/05, 11/12/04*, 8/30/04
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

ACKNOWLEDGMENT OF IDS, STATUS OF THE APPLICATION AND CLAIMS

1. The information disclosure statement (IDS) and Form PTO-1449 filed 8/30/04, 11/12/04 and 2/1/05, respectively are acknowledged, entered and considered. Claims 1-26 are now pending in the application.

OBJECTION TO TRADEMARK AND ITS USE

2. The use of the trademark "Mucomyst®" has been noted in this application. The trademark has not been capitalized, it should be capitalized whenever it appears and be accompanied by the generic terminology. Although, the use of trademark is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent its use in a manner, which might adversely affect their validity as trademark.

Further, the specification, which specifies the generic terminology should include, published product information sufficient to show that the generic terminology or the generic description are inherent in the article referred by the trademark. These description requirements are made because the nature and composition of articles denoted by trademark can change and affect the adequacy of the disclosure.

OBJECTIONS TO THE SPECIFICATION

3. The specification is objected on page 21, line 21 in the recitation "SEQ ID NOs4-12". It is believed to be typographical error because it is inconsistent with other

sequences recite din the specification. Amendment of the specification to recite "SEQ ID NOS:4-12" " would obviate this objection.

CLAIM REJECTION-35 U.S.C. § 112 2nd PARAGRAPH

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 6, 7 and 9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 6, 7 and 9 are indefinite in the recitation "....the composition is administered to the patient....." (claims 6 and 9) and "....the protein or peptide is administered to a patient....." (claim 7) because there is no proper antecedent basis for the term "administering" in claim 1, or claim 6, or claim 7 or claim 9, rather claim 1 is directed to "contacting". Appropriate clarification is required.

CLAIMS REJECTION-35 U.S.C. § 103(a)

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over White et al (U.S. Patent No. 5,985,261).

The reference of White et al ('261 patent) teaches a method to treat oxidative damage in an animal by administration of a protein having a thioredoxin active-site in reduced state that is effective to induce production of cellular manganese super oxide dismutase (MnSOD) which is induced by thioredoxin as admittedly acknowledged on page 16, lines 17-10 in the instant specification, and as such would result in treatment of oxidative damages, wherein the thioredoxin active-site comprises the amino acid sequence C-X-X-C or X-C-X-X-C-X, wherein "C" are cysteine residues and "X" any amino acid residue, and in particular, any of the standard 20 amino acid residues. Further, the '261 patent on col. 4, lines 64 to col. 5, lines 25 discloses a thioredoxin active-site comprising the amino acid sequence C-X-X-C (SEQ ID NO:1), which is identical with the sequence claimed in claim 10; X-C-X-X-C-X (SEQ ID NO:3), which is identical with the sequence claimed in claims 11, 19 and 26; X-C-G-P-C-X (SEQ ID NO:4), which is identical the claimed SEQ ID NO:2 in claims 12 and 20; and W-C-G-P-C-K (SEQ ID NO:5), which is identical with the claimed SEQ ID NO:3 in claims13 and 21. The reference states that oxidative damage refers to cellular damage that occurs as a result of the accumulation of oxygen-free radicals and other oxidative species in cells. Such oxygen-free radicals and oxidative species (e.g., hydrogen peroxide) result from reactive oxygen intermediates produced during various types of stress, caused by conditions such as lung diseases, but not limited to respiratory disease syndrome and asthma would encompass cystic fibrosis (CF). Thus, the prior art

teaches the use of thioredoxin active site in reduced state for induction of MnSOD to treat oxidative damage.

The reference of White et al shows the administration of a protein containing a thioredoxin active-site to an animal in an amount that is between about 1.5 mmoles/kg body weight of an animal to about 150 mmoles/kg body weight of an animal, wherein suitable modes of administration can include, but are not limited to, oral, nasal, intratracheal injection, inhaled, transdermal, rectal, and parenteral routes. Preferred parenteral routes can include, but are not limited to, subcutaneous, intradermal, intravenous, intramuscular and intraperitoneal routes. The protein being administered has a half-life in the animal between about 5 minutes to about 24 hours. The prior art composition is further formulated with thioredoxin reductase and/or nicotinamide-adenine dinucleotide phosphate (NADPH) for reducing thioredoxin active site of the protein (See e.g., col. 1, lines 21-51, cols. 4-11 and the claims) as directed to claims 1-26.

Thus, the prior art teaches the use of a composition containing a thioredoxin active-site in reduced state effective to treat a lung disease which may include abnormal or excessive viscosity or cohesiveness of mucus or sputum because sputum is a symptom or cause of the disease including but not limited to CF. Further, as acknowledged by Applicant on page 8 in the instant specification, it is known that lung-associated diseases such as CF would result in abnormal or excessive viscosity and/or cohesiveness of the mucus or sputum, and when such a symptom occurs, one of ordinary skill in the art would have been motivated at the time the invention was

made to use an agent taught by the prior art which would result in increasing liquefaction of the mucus or sputum.

Therefore, the prior art clearly teaches the use of a composition comprising a protein or a peptide containing a thioredoxin active-site in reduced state effective to treat lung diseases or respiratory conditions including CF which are expected to be associated with symptoms of excessive or abnormal mucus viscosity and/or cohesiveness by increasing the liquid fraction and diminishing the viscoelasity of sputum or mucus. Thus, the prior art makes obvious a method of decreasing the viscosity and/or cohesiveness of and/or increasing the liquefaction of excessively or abnormally viscous or cohesive mucus or sputum in a patient comprising administering a protein or a peptide containing thioredoxin active-site, wherein the thioredoxin active-site comprises the amino acid sequence C-X-X-C or X-C-X-X-C-X, or X-C-G-P-C-X (SEQ ID NO:2) or W-C-G-P-C-K (SEQ ID NO:3), wherein "C" are cysteine residues and "X" any amino acid residue (i.e., any of the standard 20 amino acid residues) and a composition thereof. Thus, the prior art teaches a method to increase the liquefaction of mucus or sputum in a patient such as cystic fibrosis patient by contacting the mucus or sputum with a composition comprising a protein or a peptide containing a thioredoxin active-site reduced state wherein the thioredoxin is a prokaryotic or yeast or plant or mammalian thioredoxin. Therefore, the teachings of the prior art makes prima facie obvious the treatment of CF, as well as other diseases and conditions that are associated with abnormally or excessively viscous or cohesive mucus or sputum by increasing the liquefaction of mucus or sputum, and as such,

substantially discloses the invention and renders claims 1-26 obvious, absent of factual evidence or unexpected results to the contrary.

CONCLUSION AND FUTURE CORRESPONDANCE

6. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Abdel A. Mohamed whose telephone number is (571) 272 0955. The examiner can normally be reached on First Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, CAMPELL BRUCE can be reached on (571) 272 0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Mohamed/AAM
March 3, 2003

JON WEBER
SUPERVISORY PATENT EXAMINER